

### REMARKS

The above-captioned application claims priority under 35 U.S.C. § 119(e) to United States Provisional Application Serial No. 60/181,638, filed February 10, 2000.

Claims 12 and 15-17 will be pending after entry of this Amendment. Claims 1-11 were previously canceled. Claims 12-15 stand rejected. Claims 12 and 15 have been amended. Claims 13 and 14 have been canceled. Claims 16 and 17 have been added.

#### Amendments to the Claims

Claims 12 and 15 have been amended to recite "mouse" rather than "non-human animal". In addition, claims 12 and 15 have been amended to recite a phenotype for the mouse. Support for the amendments can be found, for example, on pages 5-10, 21-25 and 29-34 of the specification. Accordingly, no new matter has been added by amending claims 12 and 15.

Dependent claims 16 and 17 have been added to recite specific allergens. Support for claims 16 and 17 can be found, for example, on pages 5-10, 22-25, 29-30 and 33-34 of the specification. Accordingly, no new matter has been added by the addition of claims 16 and 17.

#### Rejection under 35 U.S.C. § 112, first paragraph

Claims 12-15 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. Specifically, the Examiner stated that the specification, while being enabling for a transgenic mouse whose genome comprises a homozygous disruption of the endogenous CCR8 gene wherein the mouse exhibits a defective Th2 response in allergen challenged mice, does not reasonably provide enablement for other

animals. The Examiner also stated that the specification only teaches a phenotype wherein the mouse exhibits an altered Th2 response to allergen treatment.

Claims 13 and 14 have been canceled so the rejection under 35 U.S.C. § 112, first paragraph, with respect to those claims is moot.

Claims 12 and 15 have been amended to recite "mouse" rather than "non-human animal". In addition, claims 12 and 15 have been amended to recite a phenotype for the mouse. Applicant submits that claims 12 and 15, as amended, are enabled by the specification because, for example, Examples II-IV on pages 21-23 teach how to make a genetically engineered mouse whose genome lacks a CCR8 gene. In addition, pages 5-10, 22-25 and 29-34 of the specification, for example, demonstrate that said mouse exhibits a defective Th2 response when challenged with an allergen.

Applicant further submits that new claims 16 and 17, which depend from claims 12 and 15, respectively, are also enabled. For example, pages 5-10, 22-25, 29-30 and 33-34 of the specification teach allergen challenge with *Schistosoma mansoni* eggs, cockroach allergen, and ovalbumin.

Accordingly, withdrawal of the rejection of the claims under 35 U.S.C. § 112, first paragraph, is respectfully requested.

#### Rejection under 35 U.S.C. § 103

Claims 12-15 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Capecchi, "Targeted Gene Replacement", *Scientific American*, vol. 270, no. 3, pp. 34-41 (1994) ("Capecchi A") in view of Capecchi, "The New Mouse Genetics: Altering the Genome by Gene Targeting", *Trends in Genetics*, vol. 5, no. 3, pp. 70-76 (1989) ("Capecchi B") and further in view of Zingoni *et al.*, "Cutting Edge: The

Chemokine Receptor CCR8 Is Preferentially Expressed in Th2 But Not Th1 Cells", *J. Immunology*, vol. 161, pp. 547-551 (1998) ("Zingoni"). Specifically, the Examiner stated that it would have been obvious for one of ordinary skill in the art at the time the claimed invention was made to make a knockout mouse by replacing a targeted gene, as taught by Capecchi A and B, with the CCR8 gene, as taught by Zingoni.

Claims 13 and 14 have been canceled so the rejection under 35 U.S.C. § 103(a) with respect to those claims is moot. As to amended claims 12 and 15, applicant respectfully traverses the rejection and requests reconsideration of the claims.

To establish *prima facie* obviousness of a claimed invention, all of the claim limitations must be taught or suggested by the combination of the prior art. MPEP § 2143.03. In addition, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. MPEP § 2143. Put another way, the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination or modification. MPEP § 2143.01.

Capecchi A and Capecchi B both relate to the procedure for using gene targeting to generate mice with specific mutations in the nucleotide sequence of a chosen gene.

Zingoni relates to the cloning and characterization of mouse CCR8.

Accordingly, the cited references, either alone or in combination, fail to disclose or suggest a genetically engineered mouse (claim 12) or mouse embryo (claim 15) whose genome lacks a CCR8 gene, wherein the mouse exhibits a defective Th2 response when challenged with an allergen.

Thus, the combination of Capecchi A and B and Zingoni can not render claims 12 and 15 obvious; withdrawal of the rejection of claims 12-15 under 35 U.S.C. § 103(a) is respectfully requested.

#### CONCLUSION

Applicant submits that claims 12, 15, 16 and 17 are enabled by the specification and are not obvious in view of the cited references. Accordingly, reconsideration of the rejections and allowance of the claims at an early date are earnestly solicited.

If the undersigned can be of assistance to the Examiner in addressing issues to advance the application to allowance, please contact the undersigned at the number set forth below.

Respectfully submitted,



Michael G. Biro  
Reg. No. 46,556

Schering-Plough Corporation  
Patent Department  
Mail Stop K-6-1, 1990  
2000 Galloping Hill Road  
Kenilworth, NJ 07033-0530

Phone: (908) 298-5098  
Fax: (908) 298-5388